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A SIMPLE METHOD FOR PREDICTION OF THE REDUCED SCATTERING COEFFICIENT IN TISSUE-SIMULATING PHANTOMS

JIANWEI FU, GUOTAO QUAN and HUI GONG*
Britton Chance Center for Biomedical Photonics
Wuhan National Laboratory for Optoelectronics — Huazhong
University of Science and Technology, Wuhan 430074, P. R. China
**huigong@mail.hust.edu.cn*

This paper proposes a method for predicting the reduced scattering coefficients of tissue-simulating phantoms or the desired amount of scatters for producing phantoms according to Mie scattering theory without measurements with other instruments. The concentration of the scatters TiO_2 particles is determined according to Mie theory calculation and added to transparent host epoxy resin to produce phantoms with different reduced scattering coefficients. Black India Ink is added to alter the absorption coefficients of the phantoms. The reduced scattering coefficients of phantoms are measured with single integrating sphere system. The results show that the measurements are in direct proportion to the concentration of TiO_2 and have identical with Mie theory calculation at multiple wavelengths. The method proposed can accurately determine the concentration of scatters in the phantoms to ensure the phantoms are qualified with desired reduced scattering coefficients at specified wavelength. This investigation should be possible to manufacture the phantom simply in reasonably accurate for evaluation of biomedical optical imaging systems.

Keywords: Mie scattering theory; integrating sphere; optical imaging.

1. Introduction

Optimization of therapy or devices for laser applications in medicine often requires knowledge of light distribution inside biological tissue.[1] Tissue-simulating phantoms are used to simulate the optical properties of real biological tissue, and light distributions in biological tissue in optical imaging. These phantoms can be widely used in photodynamic therapy,[2] optical coherence tomography,[3] and fluorescence molecular tomography[4] to validate the algorithms, calibrate instruments, and perform quality control.

There are two different types of tissue-simulating phantoms: liquid phantoms and solid phantoms. The advantages of liquid phantoms are that the phantom materials are easy to purchase and prepare. However, liquid phantoms are difficult to preserve, and their useable lifetimes can only last for several hours to several days. Moreover, it is difficult to produce inhomogeneous liquid phantom. The requirement for inhomogeneous phantoms, like layered structure, accelerates the development of solid phantoms. The material is the most important for solid phantoms. Added with scattering materials (Intralipid) and absorption dyes (India Ink), gelatin, agar,[4,5] and polyacrylamide[6] can be cast into arbitrary shapes. These phantoms can mimic the inhomogeneous biological tissues. However, the useable lifetimes of these phantoms are usually limited to no more than two months.

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As the research going on, more and more materials are used to produce tissue-simulating phantoms, such as polyorganosiloxane,[7] polyester,[8] and epoxy resin.[9] Phantoms made of these materials have better stability and are easier to be cast into arbitrary shapes. The selection of the material is determined by the scattering material and absorption dye added. Pogue and Patterson summarized the materials, production approaches and field of applications of tissue-simulating phantoms for optical spectroscopy, imaging, and dosimetry.[10] Tuchin also explicitly presented the general approach, scattering media, and light-absorbing media for phantom preparation.[11]

After the phantom production, the optical parameters of these phantoms need to be measured with precise instruments. So it is limited by the availability and the accuracy of the instruments. Furthermore, most research groups can only measure the optical parameters of tissue in interested wavelengths, so the research of phantoms lacks of universality. A simple and reliable phantom production approach is necessary. Mie theory is rigorous solution for spherical particles irradiated by single wavelength planar light. It is a precise method to calculate the scattering property of spherical particles.[12] Mie scattering theory is usually used to validate the measurements of scattering coefficient, so it can also be fundamental of phantom production. This research proposes a simple method of producing tissue-simulating phantoms. The reduced scattering coefficients of phantoms can be predicted according to Mie calculation. To validate the accuracy of the predicted values, the phantoms are measured with single integrating sphere system. This paper shows the primary results.

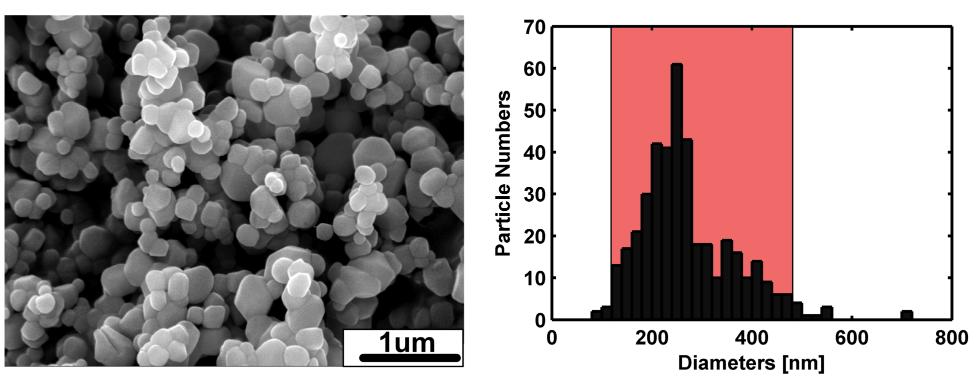
2. Materials and Methods

2.1. *Material selection*

The main materials used in phantom production are epoxy resin, nanometer-sized particles of titanium dioxide (TiO_2), and India Ink. The epoxy resin is nonscattering media with low intrinsic absorption coefficient. Its original form is transparent liquid with slight viscousness. It will polymerize at room temperature during a week. However, the polymerization will take less than 2 h at 80° C.

TiO_2 particles of which absorption coefficient is very low are used as scattering materials. The refractive index of TiO_2 is 2.55, and its density is 3.84 g/cm^3. Figure 1(a) is the electron microscopic image of nanometer-sized TiO_2 particles. Figure 1(b) is the size distribution of the diameters of 410 TiO_2 particles selected randomly. It can be seen that the TiO_2 particles used are nearly spherical and their diameters fall into 90∼710 nm. The diameters and relative numbers of particles whose diameters fall into 120∼480 nm are used in Mie calculation. Because the effect on the calculated reduced scattering coefficient of particles with other diameters is very small.

India Ink is a very stable absorption dye. Figure 2 shows the absorption coefficients μ_a of India Ink diluted with water at three different wavelengths (633, 750, and 900 nm) measured by spectrophotometer. The absorption coefficient and the volume fraction of India Ink have good linear relation in the measurement range. And according to the measurement of spectrophotometer, the absorption of India Ink is very stable. Repeatability error is less than 3%.



(a) (b)

Fig. 1. (a) Electron microscopic image of nanometer-sized TiO_2 particles and (b) The size distribution of the diameters of 410 TiO_2 particles selected randomly.

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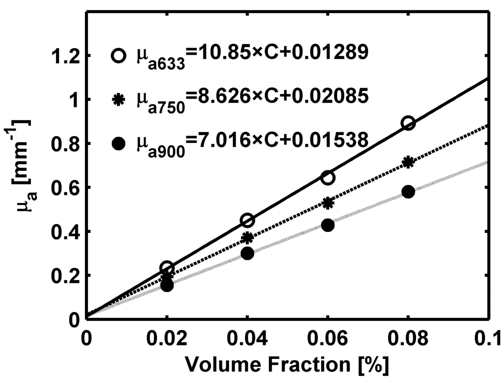

Fig. 2. The absorption coefficients of India Ink diluted with water at 633, 750, and 900 nm. C presents the volume fraction of India Ink.

2.2. *Phantom production*

The concentration of TiO_2 particles can be determined by Mie theory before producing phantoms. The formulas of Mie calculation are well-known.[13] The crucial problem of Mie calculation is to calculate Mie coefficients a_n and b_n. There are several algorithms to calculate these two coefficients.[14–17] We adopted the improved Mie scattering algorithms proposed by Wiscombe.[17] Then we can calculate the extinction efficiency Q_{ext}, scattering efficiency Q_{sca}, and scattering anisotropy factor g,

$$Q_{\text{ext}} = 2/x^2 \sum_{n=1}^{N} (2n+1) Re(a_n + b_n), \quad (1)$$

$$Q_{\text{sca}} = 2/x^2 \sum_{n=1}^{N} (2n+1)(|a_n|^2 + |b_n|^2), \quad (2)$$

$$Q_{\text{abs}} = Q_{\text{ext}} - Q_{\text{sca}}, \quad (3)$$

$$g = \frac{4}{x^2 Q_{\text{sca}}} \sum_{n=1}^{N} \left[\frac{n(n+2)}{n+1} \text{Re}(a_n a_{n+1}^* + b_n b_{n+1}^*) + \frac{(2n+1)}{n(n+1)} \text{Re}(a_n b_n^*) \right], \quad (4)$$

where, x is the size parameter of scatters, it is determined by particle diameter D and light wavelength λ: $x = \pi D/\lambda$. a_n and b_n depend on the complex refractive index $m(= m_{Re} - i m_{\text{Im}})$. They are expressed in terms of spherical Bessel functions. The reduced scattering coefficient extrapolated to a volume fraction of 100%,

$$\sigma' = \frac{3Q_{\text{sca}}}{4r_p}(1-g), \quad (5)$$

will be called the specific coefficients here.[18] The reduced scattering coefficient is proportional to the volume fraction (dimensionless) of the particles,

$$\mu_s' = \sigma' v_p = \pi r_p^2 Q_{\text{sca}}(1-g)N, \quad (6)$$

where, N represents the particle density (numbers of particles in per unit volume of phantom). The determination of the concentration of TiO_2 particles according to desired μ_s' is straightforward.

The phantom production process can be separated into several steps as follows: first, the epoxy resin is prepared by mixing four components (ERL-4221 (10 g), DER-736 (6.8 g), NSA (26 g), DMAE (0.2 g)). ERL-4221 (3,4-epoxycyclohexyl carboxylate) with low viscosity is easy to operate. DER-736 (diglycidyl ether of a polypropylene glycol) also has low viscosity. It is used to alter the hardness of the phantoms. NSA (nonenylsuccinic anhydride) is a special kind of hardener. DMAE (dimethylaminoethanol) is used as activator to shorten the polymerization time. The mixture is stirred with magnetic stirrer for at least one hour at room temperature to make sure the mixture is mixed sufficiently. Second, certain amount of TiO_2 particles and India Ink are added into the mixture. The mixture is stirred with magnetic stirrer for at least 2 h. In the end, the mixture is poured into a mold and the mold is put into dry oven. Staying still for at least 2 h at 80°C, the phantom would polymerize completely and its optical parameters would be stable. It is crucial to accurately control the amount of TiO_2 particles and India Ink. Here, we pour the TiO_2 into a glass beaker containing alcohol and break up the clustered particles with ultrasound. Then the mixture is stirred into homogeneous suspension and desired amount of suspension is added into epoxy resin with pipette. India Ink is usually diluted with water and then added into epoxy resin with pipette. The water and alcohol will evaporate during polymerization, so the ratio of each material can be ensured. A set of phantoms qualified with different μ_a and μ_s' can be produced with this method.

2.3. *Optical parameter measurement*

The optical parameters of phantoms are measured with the 150 mm integrating sphere accessory of Lambda 950 VU/Vis/NIR Spectrophotometers for high precision reflectance and scattered transmittance measurements. The reflectance/transmittance can be measured with samples attached directly to the reflection/transmission sample holder, as is demonstrated in Fig. 3. The optical

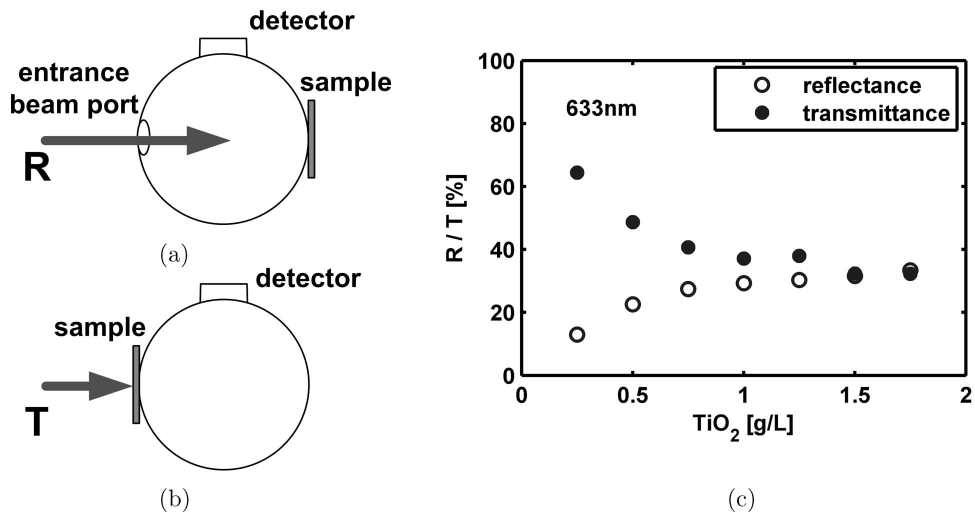

Fig. 3. The schematic shows how to measure the reflectance (a) and transmittance (b) with one integrating sphere and the reflectance and transmittance measured at 633 nm for seven phantoms.

parameters can be obtained with a light propagation model when the thickness of sample is known. Here we adopt the Inverse Adding-doubling (IAD) algorithm (Prahl, 2007). The anisotropy factor g of TiO_2 particles used at 633, 750, and 900 nm are, respectively, 0.629, 0.625, and 0.587 according to Mie calculation. These three values are used as inputs of IAD program to calculate the μ_a and μ_s' of phantoms.

3. Results

Seven phantoms were produced with the method aforementioned. The concentration of TiO_2 particles in these phantoms were, respectively 0.25, 0.5, 0.75, 1, 1.25, 1.5, 1.75 g/L (volume fraction: 0.065‰, 0.13‰, 0.195‰, 0.26‰, 0.325‰, 0.39‰, 0.456‰), while the volume fraction of India Ink hold constant (0.0125%). To fulfill the requirement of integrating sphere system, all phantoms were cast into slab geometry of which the size is about $50 \times 50 \times 1\,\text{mm}^3$. Each phantom was sandwiched by two glass sheets of which the size are $60 \times 60 \times 1\,\text{mm}^3$. After polymerization completely, the diffuse reflectance and transmittance were measured with single integrating sphere system. Then the measured μ_a and μ_s' were calculated by IAD program.

The μ_s' and μ_a of these phantoms at three different wavelengths are shown in Fig. 4. Figures 4(a), 4(c), and 4(e) respectively show the measurements

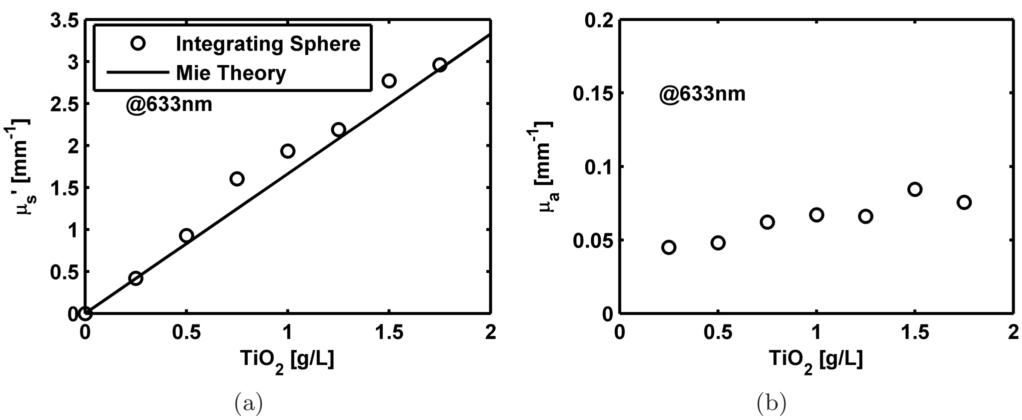

Fig. 4. μ_s' and μ_a vs the concentration of TiO_2 particles for seven phantoms at three different wavelengths. (a), (c), (e), ∘ represent, respectively, the measured μ_s' by single integrating sphere system at 633, 750, and 900 nm, the line indicates the predicted values by Mie theory. (b), (d), (f), ∘ represent, respectively, the measured μ_a by single integrating sphere system at 633, 750, and 900 nm.

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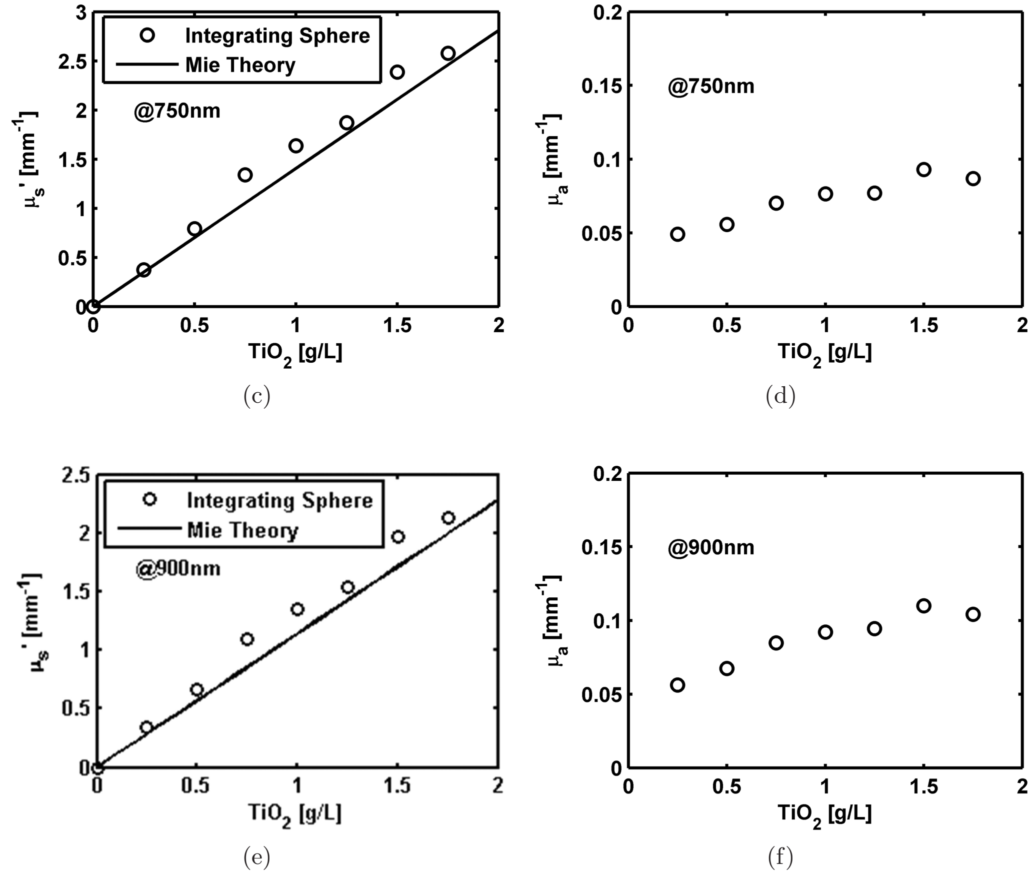

Fig. 4. (*Continued*)

of μ_s' at 633, 750, and 900 nm and the predicted μ_s'. There is a good agreement between the measurements and predicted values. The predicted μ_s' are calculated by Mie calculations. The relative numbers of every 10 nm-interval are counted and used to calculate the predicted μ_s', As is demonstrated in Fig. 1. We take di+5 nm as the diameters of the particles whose diameters fall into interval (di, di+10 nm) in Mie calculations. Figures 4(b), 4(d), and 4(f) respectively show the measurements of μ_a at 633, 750, and 900 nm.

The μ_a and μ_s' of these phantoms were measured again with single integrating sphere system in one month. The comparison between two

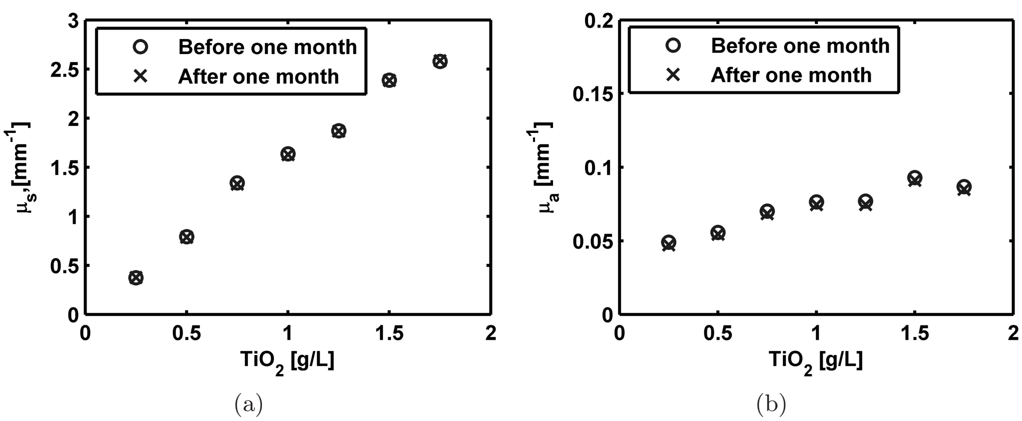

Fig. 5. The stability of (a) μ_s' and (b) μ_a of phantoms at 750 nm. (○ represents the measurements when the phantoms were just polymerized completely, × represents the measurements after a month.)

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measurement sets is shown in Fig. 5. The variation of μ_a is less than 0.07%, while that of μ_s' is less than 0.002%. The optical properties of these phantoms are very stable.

4. Discussion and Conclusion

This research proposes a simple method to produce tissue-simulating phantoms. The reduced scattering coefficients of phantoms can be predicted by Mie theory. In order to validate this method, we measured the optical parameters of a set of phantoms with single integrating sphere system. The results show that the measurements are in accordance well with the predicted values. The advantage of this method is that the concentration of TiO_2 particles can be determined by Mie theory according to the desired μ_s' at a certain wavelength. So phantoms with desired μ_s' can be produced. And the μ_s' at other wavelengths can also be calculated, so it can break the limits of measurable wavelength range of most instruments. The phantoms produced can be used in optical imaging, such as fluorescence molecular tomography, to validate the algorithms, calibrate instruments, and perform quality control.

The absorption coefficients of phantoms can also be measured by single integrating sphere system. As shown in Fig. 4, although the volume fraction of India Ink keep constant, measured absorption coefficients are different between the phantoms with different TiO_2 concentrations. This may be caused by several possible reasons referred as follows: first, the absorption coefficients of phantoms may be influenced by TiO_2 particles. So we can see that the higher the TiO_2 concentration is, the larger the absorption coefficient is. Second, when the diffused transmission light is measured, a fraction of the light that pass through phantoms would be reflected by the inner wall of integrating sphere and lost. Then the measured transmittance would be smaller. The IAD method would overestimate the absorption because of light losses.[19]

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References

1. D. Zhu, Q. M. Luo, J. A. Cen, "Effects of dehydration on the optical properties of in vitro porcine liver," *Laser Surg. Med.* **33**(4), 226–231 (2003).
2. B. W. Pogue, L. Lilge, M. S. Patterson, B. C. Wilson, T. Hasan, "Absorbed photodynamic dose from pulsed versus continuous wave light examined with tissue-simulating dosimeters," *Appl. Opt.* **36**(28), 7257–7269 (1997).
3. J. G. Fujimoto, C. Pitris, S. A. Boppart, M. E. Brezinski, "Optical coherence tomography: An emerging technology for biomedical imaging and optical biopsy," *Neoplasia* **2**, 9–25 (2000).
4. Y. Y. Tan, H. B. Jiang, "DOT guided fluorescence molecular tomography of arbitrarily shaped objects," *Med. Phys.* **35**(12), 5703–5707 (2008).
5. R. Cubeddu, A. Pifferi, P. Taroni, A. Torricelli, G. Valentini, "A solid tissue phantom for photon migration studies," *Phys. Med. Biol.* **42**(10), 1971–1979 (1997).
6. M. N. Iizuka, M. D. Sherar, I. A. Vitkin, "Optical phantom materials for near infrared laser photocoagulation studies," *Laser. Surg. Med.* **25**(2), 159–169 (1999).
7. G. C. Beck, N. Akgun, A. Ruck, R. Steiner, "Design and characterization of a tissue phantom system for optical diagnostics," *Laser. Med. Sci.* **13**(3), 160–171 (1998).
8. M. Firbank, D. T. Delpy, "A design for a stable and reproducible phantom for use in near infra-red imaging and spectroscopy," *Phys. Med. Biol.* **38**, 847–853 (1993).
9. J. Zhao, H. S. Ding, Z. Y. Zhao, J. Du, "Phantoms with tissue-like optical properties for use in near-infrared spectroscopy and imaging," *J. Optoelectron. Laser* **16**(4), 496–500 (2005).
10. B. W. Pogue, M. S. Patterson, "Review of tissue simulating phantoms for optical spectroscopy, imaging and dosimetry," *J. Biomed. Opt.* **11**(4), 041102-1–16 (2006).
11. V. V. Tuchin, "Handbook of Optical Biomedical Diagnostics," SPIE Press, Bellingham (2002).
12. Y. Yang, Z. X. Zhang, D. Z. Jiang, "Numerical calculation of Mie scattering," *J. Appl. Opt.* **18**(4), 17–19 (1997).
13. C. F. Bohren, D. R. Huffman, *Absorption and Scattering of Light by Small Particles*, Wiley-Interscience, New York (1983).
14. Z. Zhu, M. Ye, Y. Lu, Y. G. Lu, T. Hu and S. M. Wang, "High precise algorithm of Mie scattering in the particle sizing by light scattering," *J. Optoelectron. Laser* **10**(2), 135–138 (1999).
15. G. Zheng, X. S. Cai and N. N. Wang, "Numerical calculation of Mie scattering," *Appl. Laser* **12**(5), 220–222 (1992).

16. J. Q. Shen and L. Liu, "An improved algorithm of classical Mie scattering calculation," *China Powder. Sci. Technol.* **4**, 1–5 (2005).
17. W. J. Wiscombe, "Improved Mie scattering algorithms," *Appl. Opt.* **19**(9), 1505–1509 (1980).
18. G. C. Beck, N. Akgun, A. Ruck and R. Steiner, "Developing optimized tissue phantom systems for optical biopsies," *SPIE* **3197**, 76–85 (1997).
19. D. Zhu, W. Lu, S. Zeng and Q. Luo, "Effect of light losses of sample between two integrating spheres on optical properties estimation," *J. Biomed. Opt.* **12**(6), 064004 (2007).

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